REMARKS

The Office Action dated January 15, 2003 presents the examination of claims 3-5, 7-8, and 13-15. Claims 13 and 14 are amended. Support for the recitation of "using PCR method" in claim 13 is found on page 14, lines 26-32, and page 15, lines 1-6 of the specification. Other claim amendments are merely to delete terms and/or phrases. No new matter is inserted into the application.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner maintains the rejection of claims 3-5, 7-8, and 13 under 35 U.S.C. § 112, first paragraph for allegedly containing new matter not originally described in the specification. Applicant respectfully traverses. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner asserts that there is no support in the specification for "3.6×10^{-6} μg." In order to overcome the rejection, "3.6×10^{-6} μg" is deleted from independent claim 13.

The Examiner also states that requiring the value of A and B to be set in terms of μg also raises new matter. Again, in order to overcome the rejection, "in μg" is deleted from independent claim 13, as well as independent claim 14.

Applicant respectfully submits that the claims do not contain any subject matter not present in the specification as filed. Thus, withdrawal of the instant rejection is respectfully requested.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 3-5, 7-8, and 13-15 for allegedly being indefinite. Applicant respectfully traverses. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Specifically, the Examiner asserts that the present method allows the skilled artisan to estimate a theoretical detection limit, but does not allow the skilled artisan to quantify the amount of non-labeled sample DNA that has hybridized to the labeled sample DNA. Applicant respectfully disagrees.

It is apparent from the specification and claim 13 that the quantification recited in claim 13 represents the fractional equivalent of the percentage of the mutated or polymorphic target DNA in the sample DNA. Thus, the skilled artisan can quantify the amount of non-labeled sample DNA that has hybridized to the labeled sample DNA by use of the fractional proportion. A direct amount is

not necessary.

For this reason, Applicant respectfully submits that claims 3-5, 7-8, and 13-15 distinctly claim the invention such that the requirements of 35 U.S.C. § 112, second paragraph are met. Withdrawal of the instant rejection is respectfully requested.

Rejection under 35 U.S.C. § 102/103

The Examiner rejects claims 3-5, 7-8, and 13-15 under 35 U.S.C. § 102(b) for allegedly being anticipated by, or in the alternative, under 35 U.S.C. § 103(a) for allegedly being obvious over Oka et al. (Nucleic Acids Research 22(9):1541-1547 (1994). Applicant respectfully traverses. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Oka et al. discloses a method for detecting known congenital mutations in chromosome DNA. In this method, Oka et al. discloses that it is important to distinguish between the three genotypes of homozygous wild type, heterozygote, and homozygous mutant. In the method of Oka et al., the combination of a labeled sample of a wild type and an unlabeled sample is utilized. In addition, Oka et al. describes a method for detecting the unknown allele type to the degree that the small amount of 10% of mutant genes can be

detected. The amount of the mutant genes is estimated/calculated from the absorbance obtained by this process. According to the method disclosed in Oka et al., since it is difficult to anticipate the sequence of mutant genes, it is difficult to prepare and use a labeled sample having the same sequence as the mutant genes. As a result, only the mutant genes having a different sequence from the labeled sample can be detected.

On the other hand, in the present invention, the assay is conducted by adding an excessive amount of non-labeled sample DNA to the labeled standard DNA to promote competitive hybridization, and measuring the resulting hybridizate for the label intensity to evaluate the extent to which the labeled standard DNA has been diluted. In this process, the type of the target DNA which is the same as the labeled standard DNA and which may be present in the sample DNA (i.e. the type of the nucleic acid including the gene mutation or polymorphism) is estimated and the detection limit for the target DNA including the gene mutation or polymorphism is selected; and the sample DNA of certain excessive amount is added to the labeled standard DNA which has been selected according to the estimated mutation and polymorphism. In short, the present invention includes as an important feature the adjustment of the

mixed ratio of a labeled sample DNA and an unlabeled DNA in order to set the degree of the detection limit from the characteristics of the target DNA to be conducted at the detection sensitivity within the optimal region corresponding to the content of the target DNA. The detection limit of the target DNA in the sample DNA is appropriately selected depending on the type of the target DNA. For instance, the detection limit is 50% in the case of heterozygote, and approximately 1% in the case of cancer gene because of the existence of the large amount of the DNA based on germinal cells around the cancer gene. It is further necessary to adjust the detection limit of the cancer gene in a minute amount (less than 1%) when the gene is detected from blood. In this way, in the present invention, it is important to set the mixed ratio in accordance with the characteristics of a variety of target DNAs.

Therefore, the process of Oka et al. quite differs from the process of the present invention and the cited reference does not disclose or suggest the claimed concept, that is, the mixed ratio of a labeled sample DNA and an unlabeled DNA is adjusted and set by expecting the degree of the detection limit to be conducted at the detection sensitivity within the optimal region corresponding to the content of the target DNA.

Therefore, the present invention is patentable over Oka et al. Withdrawal of the instant rejection is respectfully requested.

Rejection under 35 U.S.C. § 102(f)

The Examiner rejects claims 3-5, 7, 8, and 13-15 under 35 U.S.C. § 102(f) because Applicant did not allegedly invent the claimed subject matter. Applicant respectfully traverses. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner points out that the authors of Oka et al. are different from the named inventor of the present application. Applicant respectfully submits that this point is irrelevant, since Oka et al. does not anticipate the present invention as explained above. Therefore, withdrawal of the instant rejection is respectfully requested.

Summary

Applicant respectfully submits that the above amendments and remarks alleviate the Examiner's outstanding rejections such that the present invention is in a condition for allowance. Favorable action and early allowance of the claims are respectfully

requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at 703/205-8000 in the Washington Metropolitan Area.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment: Version with Markings to Show Changes Made

(Rev. 02/12/01)

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims:

The following claims are amended:

13. (Five Times Amended) A nucleic acid assay process for identifying and/or quantifying a mutation or polymorphism in a double stranded sample DNA prepared by amplification of a particular region of an analyte nucleic acid using PCR method which is present in a specimen, comprising the steps of:

providing labeled standard DNA having a nucleotide sequence the same as a mutated or polymorphic target DNA of interest, wherein said labeled standard DNA comprises a double stranded nucleic acid having a site capable of binding to a solid support on one strand and a detectable label on the other strand;

amplifying said particular region of said analyte nucleic acid which is present in said specimen to prepare said double stranded sample DNA for competitive hybridization, wherein said sample DNA comprises both mutated or polymorphic target DNA and wild-type DNA in an amplifiable amount;

selecting a detection limit for said mutated or polymorphic target DNA, wherein when the detection limit for the target DNA present in said sample DNA is A/B, the excessiveness of said sample

DNA is at least B/A, and wherein A/B is the fractional equivalent of the percentage of said mutated or polymorphic target DNA content in the sample DNA [and A is at least 3.6×10^{-6} μg];

adding an excessive amount [in μg] of said sample DNA to said labeled standard DNA, to allow competitive hybridization to take place between said mutated or polymorphic target DNA and labeled standard DNA under conditions which allow for hybridization of at least some of said labeled standard DNA and under conditions wherein non-target sample DNA does not hybridize with said labeled standard DNA, wherein the excessiveness of said sample DNA added to said labeled standard DNA in the competitive hybridization is calculated as the value of B/A,

detecting the hybridized labeled standard DNA by utilizing said detectable label and said site capable of binding to a solid support; and

evaluating the degree of exchange that occurred during competitive hybridization of the complementary strands between said sample DNA and said labeled standard DNA.

14. (Amended) A nucleic acid assay process for identifying and/or quantifying a mutation or polymorphism in a double stranded

sample DNA prepared by amplification of a particular region of an analyte nucleic acid which is present in a specimen, comprising the steps of:

providing labeled standard DNA having a nucleotide sequence the same as a mutated or polymorphic target DNA of interest, wherein said labeled standard DNA comprises a double stranded nucleic acid having a site capable of binding to a solid support on one strand and a detectable label on the other strand;

amplifying said particular region of said analyte nucleic acid which is present in said specimen to prepare said double stranded sample DNA for competitive hybridization, wherein said sample DNA comprises both mutated or polymorphic target DNA and wild-type DNA in an amplifiable amount;

selecting a theoretical value [in μg] for the amount of said mutated or polymorphic target DNA in said sample DNA, wherein the amount [in μg] of said mutated or polymorphic target DNA is expressed as A, and the total amount [in μg] of said sample DNA is B, such that A/B is the fractional equivalent of the percentage of said mutated or polymorphic target DNA content in the sample DNA;

adding an excessive amount [in μg] of said sample DNA to said labeled standard DNA, to allow competitive hybridization to take

place between said mutated or polymorphic target DNA and labeled standard DNA under conditions which allow for hybridization of at least some of said labeled standard DNA and under conditions wherein non-target sample DNA does not hybridize with said labeled standard DNA, wherein the excessiveness of said sample DNA added to said labeled standard DNA in the competitive hybridization is calculated as the value of B/A,

detecting the hybridized labeled standard DNA by utilizing said detectable label and said site capable of binding to a solid support; and

evaluating the degree of exchange that occurred during competitive hybridization of the complementary strands between said sample DNA and said labeled standard DNA.